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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,077	ERBE ET AL.	
	Examiner	Art Unit	
	Allison M Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

Claims 1-78 are pending in the current application.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: BIOCOMPATIBLE BONE GRAFT MATERIAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 44 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The term "second material" in claim 44 is regarded as insufficient written description of the bone graft material composition; therefore applicant has failed to clearly convey the subject matter that they are claiming. Because applicant has failed to disclose what components the bone graft material comprises, beyond a first polymeric material and an unknown "second material," applicant has failed to put the public in possession of the claimed invention. *See Eli Lilly,* 119F. 3d. at 1568, 43 USPQ2d at 1406.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17, 21-23, 30, 31, 41, 42, 44 and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 1 and its dependents are directed to a biocompatible bone graft material comprising a biocompatible, resorbable polymer and the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion. It is not clear how many ingredients applicant is intending to claim. It is not clear if the oxidation-reduction reaction product is the product of the reaction of: at least one metal cation + at least one oxidizing agent + at least one oxidizable precursor anion; or if the oxidation-reduction reaction product is the product of the reaction of: at least one metal cation + at least one oxidizing agent, and then the "at least one oxidizable precursor anion" is a third component. It would be remedial to simply list the components in separate lines, for example:

"A biocompatible bone graft material comprising:

a) a biocompatible, resorbable polymer and

b) the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion.

Applicant's claims 16, 17, 30, 31, 41 and 42 require the graft material to further comprise a mesh or plate. It is not clear how the graft material further comprises a mesh or plate, as the material has no shape or form. It appears as if a *formed graft* could further comprise a mesh or plate, but not the *graft material*, per se.

Claims 21-23 recite the limitation "said reaction product" in the first line of each of the claims. There is insufficient antecedent basis for this limitation in claim 18; in claim 18 calcium phosphate is claimed.

Applicant's claim 44 is directed to a biocompatible graft comprising a biocompatible, resorbable substantially homogenous blend of a first polymeric material and a second material having interconnected macro-, meso- and microporosity. The description of the "second material" is insufficient to particularly and distinctly claim applicant's invention. Furthermore, it is not clear if the "second material" has interconnected macro-, meso- and microporosity, or if the complete graft has interconnected macro-, meso- and microporosity.

Applicant's claim 72 is self-dependent. The metes and bounds of the claim cannot be determined. It appears applicant intended to refer to the graft of claim 71; examination has been conducted as such.

Please note that the language of a claim must make it clear what subject matter the claim encompasses to adequately delineate its "metes and bounds." See, e.g., the following decisions: In re Hammack, 427 F 2d. 1378, 1382, 166 USPQ 204, 208 (CCPA 1970); In re Venezia 530 F 2d. 956, 958, 189 USPQ 149, 151 (CCPA 1976); In re Goffe, 526 F 2d. 1393, 1397, 188 USPQ 131, 135 (CCPA 1975); In re Watson, 517 F 2d. 465, 477, 186 USPQ 11, 20 (CCPA 1975); In re Knowlton 481 F 2d. 1357, 1366, 178 USPQ 486, 492 (CCPA 1973). The courts have also indicated that before claimed subject matter can properly be compared to the prior art, it is essential to know what the claims do in fact cover. See, e.g., the following decisions: In re Steele, 305 F 2d. 859, 134 USPQ 292 (CCPA 1962); In re Moore 439 F 2d. 1232, 169 USPQ 236 (CCPA 1969); In re Merat, 519 F 2d. 1390, 186 USPQ 471 (CCPA 1975).

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 13-15, 18, 28, 29, 50 and 59-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Piez et al (US Patent 4,795,467).

Piez et al teach bone grafts comprised of calcium phosphate mineral preparations and collagen (See col. 2, ln 32-35). The calcium phosphate mineral material can include a variety of forms of calcium phosphate, including the brand SYNTHOGRAFT, Bachand defines SYNTHOGRAFT to be beta tricalcium phosphate (See col. 2, ln 59-68 & Bachand, Pg. 2). The collagen is preferably from the same individual or from bovine sources, in order to reduce immune responses and increase biocompatibility (See col. 1, ln 30-35) (Claims 1, 2, 13 and 18). Piez et al also teach a method for restoring or repairing bone comprising placing into a bony space the bone graft material comprised of calcium phosphate and collagen (See col. 2, ln 48-52, col. 5, ln 23-35 & col. 7, ln 4-48) (Claims 50 and 59). Piez et al teach bone marrow, blood and saline can also be applied to the graft material (See col. 5, ln 15-21) (Claims 14, 28 and 60). Additionally, Piez et al teach the graft material can be loaded into a container to provide a desired shape, Piez et al specifically teach block, square, and sheet shapes (See col. 4, ln 67-col. 5, ln 2) (Claims 15, 29 and 61).

Applicant's claims 1 and 50 are drawn to a biocompatible bone graft material comprising a biocompatible, resorbable polymer and the reaction product of the oxidation-reduction reaction of at least one meal cation, at least one oxidizing agent and at least one oxidizable precursor anion. Claims 13 and 59 require the reaction product to be calcium phosphate. However, the oxidation-reduction reaction product as claimed is determined to be product-by-process claims. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Therefore, though Piez et al does not disclose the same

method of forming the calcium phosphate, the resulting calcium phosphate is the same as that used in the graft of the current application, and the graft material, method of forming the graft, and the graft itself are the same as in the current application, as taught above. Therefore the reference anticipates the claimed subject matter.

Claims 1, 2, 13 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugihara et al (US Patent 5,238,491).

Sugihara et al teach a biocompatible bone grafting material for medical and dental use comprising calcium phosphate, a hardening liquid and collagen (See col. 1, ln 59-col. 2, ln 2) (Claims 1, 2, 13, 18). The calcium phosphate comprises a mixture of alpha tricalcium phosphate and beta tricalcium phosphate (See col. 2, ln 37-47).

As taught above, the oxidation-reduction reaction product as claimed in claim 1 is determined to be a product-by-process claim and though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. Therefore, though Sugihara et al do not disclose the same method of forming the calcium phosphate, the resulting calcium phosphate is the same as that used in the graft of the current application, and the graft material, method of forming the graft, and the graft itself are the same as in the current application, as taught above. Therefore the reference anticipates the claimed subject matter.

Claims 1, 12, 13, 15, 44 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Sapiesko et al (US Patent 6,383,519).

Sapiesko et al teach porous, shaped, inorganic bodies comprising biocompatible, resorbable polymers, such as gelatin, and the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent and at least one oxidizable precursor anion (See col. 4, ln 3-34) (Claim 1). In

preferred embodiments the oxidation-reduction reaction product is beta tricalcium phosphate (See col. 8, ln 28-46). The composition of Sapiesko et al can be used as bone graft material (See col. 5, ln 7-9). The bone graft material of Sapiesko et al exhibits macro-, meso- and microporosity, and the material has a pore volume of at least 75% (See col. 9, ln 39- col. 10, ln 25) (Claims 12, 13, 44 and 63). The graft material can be wetted with blood or bone marrow cells prior to implantation (See col. 24, ln 18-30) (Claim 14). The graft material can be formed into a variety of shapes, including blocks, disks, cylinders, or sleeves for orthopedic surgery (See col. 12, ln 1-13; col. 23, ln 63-65; col. 42, ln 64-67) (Claims 15 and 63). Therefore the reference anticipates the claimed subject matter.

Claims 1-5, 13, 14, 18-20, 28, 50-52 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Cornell et al (J Ortho Trauma, 1991).

Cornell et al teach use of Collagraft (Zimmer Corporation, Warsaw, IN) as a bone graft material for filling open comminuted fractures by placing the Collagraft into the opened bony space. Collagraft comprises a composite of porous calcium phosphate and collagen (See Pg. 2) (Claims 1-2, 13, 18, 50 and 59). The calcium phosphate composite consists of 65% hydroxyapatite and 35% tricalcium phosphate. The pore volume is approximately 70%. The collagen is highly purified, completely resorbable, fibrillar bovine-derived collagen; it is 95% Type I bovine collagen (See Pg. 2 and 5) (Claims 3-5, 19-20 and 51-52). The Collagraft bone graft material is wetted with bone marrow aspirate before implantation (Claims 14 and 28).

As taught above, the oxidation-reduction reaction product as claimed in claims 1 and 50 is determined to be a product-by-process claim and though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. Therefore, though Cornell et al do not disclose the same method of forming the calcium phosphate, the resulting calcium phosphate is the same as that used in the graft of the prior art, and the graft material, method of forming

the graft, and the graft itself are the same as in the current application, as taught above. Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-12, 15, 19-27, 29, 32-40, 44-48, 51-58, 61, 63, 67-71 and 74-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piez et al (US Patent 4,795,467), in light of Bachand.

Piez et al teach bone grafts comprised of calcium phosphate mineral preparations (which applicant calls the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion) and collagen (which applicant calls a biocompatible, resorbable polymer) (See col. 2, ln 32-35). The calcium phosphate mineral material can include a variety of forms of calcium phosphate, including beta tricalcium phosphate SYNTHOGRAFT; SYNTHOGRAFT is a commercially available form of beta tricalcium phosphate (See col. 2, ln 59-68 & Bachand, Pg. 2). The collagen is preferably obtained from the same individual or from bovine sources in order to reduce immune responses and increase biocompatibility (See col. 1, ln 30-35). Piez et al also teach a method for restoring or repairing bone comprising placing into a bony space the bone graft material comprised of calcium phosphate and collagen (See col. 2, ln 48-52, col. 5, ln 23-35 & col. 7, ln 4-48). Piez et al teach bone marrow, blood and saline can also be applied to the graft material (See col. 5, ln 15-21). Additionally, Piez et al teach the graft material can be loaded into a container to provide a desired shape, Piez et al specifically teach block, square, and sheet shapes (See col. 4, ln 67-col. 5, ln 2).

Piez et al teach the mineral blocks, made from powdered tricalcium phosphate or hydroxyapatite, used to form the bone grafts to be porous (See col. 5, ln 36-43); however, they do not specifically teach the bone grafts to have macro-, meso- or microporosity. The size range of the pores is a result effective variable that would routinely be optimized by one of ordinary skill in the art. Piez et al clearly indicate that the mesh size of the tricalcium phosphate and/or hydroxyapatite particles used in the claimed composition directly effects the size of the pores (See col. 5, ln 63-68). Therefore, it would have been obvious to one of ordinary skill in the art to use a mineral particles with varied mesh sizes in order to achieve macro-, meso- and microporosity in the bone graft material of Piez et al, as described above (Claims 12, 27, 32, 39, 44, 48, 58, 63, 67, 71 and 74). One of ordinary skill in the art would have been motivated to use mineral particles with varied mesh sizes in order to create a mineral block, for use in a bone graft, with macro-, meso- and microporosity, in order to better replicate natural, porous bone structure for bone and blood cells to invade. One would have expected success because Piez et al teach a method for producing mineral blocks from particles of beta tricalcium phosphate and/or hydroxyapatite and collagen, and coating the mineral blocks in collagen to produce bone graft materials and Piez et al teach that the mesh size of the mineral particles directly effects the resulting pore size; therefore because pore size is a result effective variable, one would have expected success creating macro-, meso- and microporosity by using particles of varied mesh size. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use an appropriate mixture of particle sizes to achieve at least 70% porosity in the graft of Piez et al (Claim 47). One of ordinary skill in the art would have been motivated to achieve at least 70% porosity in the graft of Piez et al because the degree of porosity is directly related to the amount of natural bone recolonization. Natural osteocytes will grow into the pores in the bone graft, using the bone graft as a matrix; therefore increased porosity equates to an increased number of bone cells that can eventually be present in the graft. One would have expected success because Piez et al teach the porosity of the graft depends directly from the mesh size of the

mineral particles used; one of ordinary skill in the art would have been able to determine the appropriate mix of mesh sizes to achieve 70% porosity as a matter of routine optimization.

Piez et al teach the bone graft composition should comprise approximately 75-98% by weight calcium phosphate mineral component and approximately 25-2% by weight collagen (See col. 4, ln 57-65). In example 1, Piez et al produce bone graft material by combining 65% hydroxyapatite with 35% collagen; hydroxyapatite was used in place of tricalcium phosphate, as Piez et al teach either mineral can be used (See col. 7, ln 4-48 & col. 2, ln 32-40). Piez et al use ZYDERM collagen, which is 6.5% collagen in saline; therefore the final bone graft composition is 2.3% collagen by weight (Claims 9-12, 24-26, 36-38 and 55-57). However, it would have been obvious to one of ordinary skill in the art to develop the bone graft material of Piez et al using anywhere between 75-98% by weight beta tri-calcium phosphate (i.e. SYNTHOGRAFT) and 2-25% collagen (mass ratio of beta-tricalcium phosphate and collagen is (75-98):(25-2); therefore the mass ratio can be 70:30, 80:20 or 90:10). Piez et al teach that the ratio of calcium phosphate to collagen is a direct result of the mesh size of the mineral particles used; the particle size directly effects the level of porosity, and therefore the amount of collagen that fills the pores. Larger mesh size creates more pore space, and therefore a greater amount of collagen present in the graft. The mesh size of the mineral particles is a result effective variable that would routinely be optimized by one of ordinary skill in the art to obtain the desired calcium phosphate to collagen ratio (See col. 5, ln 63-68). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to alter the mesh size of the particles to create bone grafts with calcium phosphate to collagen ratios of 70:30, 80:20 or 90:10 (Claims 6-11, 21-26, 35-38, 46, 53-57, 68-69 and 77-78). One of ordinary skill in the art would have been motivated to manipulate the mesh size of the mineral particles in order to increase or decrease the ratio of calcium phosphate to collagen in order to alter the rigidity of the graft material, within the range of about 75-98% by weight calcium phosphate mineral component and about 25-2% by weight collagen, as taught by Piez et al. For example, one of ordinary skill in the art would

desire a high calcium phosphate to collagen ratio in order to produce a more rigid graft material, for graft use in long bones or other load bearing bone grafts. A lower calcium phosphate to collagen ratio would be desirable in grafts where load bearing capabilities are not immediately necessary, for instance cranial grafts do not need to be able to withstand the weight of the body, rather a higher amount of resorbable collagen would be tolerable, then the resorbable collagen would eventually be replaced with a greater number of natural bone cells. One would have expected success because Piez et al teach that the ratio of calcium phosphate to collagen can be routinely optimized by one of ordinary skill in the art by manipulating the mesh size of the mineral particles (See col. 5, ln 63-68).

Though Piez et al teaches the collagen can come from a bovine source, they do not teach a specific kind or concentration of any particular type of bovine collagen. However, they do teach that purified atelopeptide fibrillar reconstituted collagen is suitable for their bone graft material (See col. 4, ln 41-42). Piez et al also teach type I collagen, derived from bones, is the most common type of collagen, and they teach a method to remove the telopeptides from common collagen to produce "atelopeptides." (See col. 3, ln 17-col. 4, ln 15). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use fibrillar type I bovine collagen in the bone graft material of Piez et al because Piez et al teach bovine collagen has low immune response when used in humans, they teach type I collagen is the most common type of collagen, easily found in bone sources, and Piez et al teach a method using proteolytic enzymes to remove the telopeptides from type I collagen to produce the desired "atelopeptide" collagen used in their material (Claims 3-5, 19-20, 33, 45, 48 and 51-52). It would further have been obvious to one of ordinary skill in the art at the time the invention was made to use substantially pure fibrillar type I bovine collagen, and therefore at least 85% type I bovine collagen, in order to prevent impurities that may cause immunologic reactions. One of ordinary skill in the art would have been motivated to use at least 85% type I bovine collagen as the collagen source because Piez et al teach that bovine collagen has low immune response when used in humans, and they teach that type I

collagen, derived from bones, is the most common type of collagen; therefore substantially pure type I bovine collagen would be easy to obtain. One would have expected success because Piez et al teach that atelopeptide fibrillar collagen is suitable for use in the bone graft material, and they provide a method to remove the telopeptides.

Piez et al do teach the graft material can be loaded into a container to provide a desired shape, Piez et al specifically teach block, square, and sheet shapes (See col. 4, ln 67-col. 5, ln 2); however, it would have been obvious to one of ordinary skill in the art at the time the invention was made to form the graft into any desired shape, including a cylinder, disk, a sleeve shape or a half sleeve shape, wherein the cross section of the sleeve is in the shape of a crescent moon, semi-sphere, semi-tubular, torus, or in a shape to conform to the acetabulum or any other desired anatomical tissue structure (Claims 15, 29, 40, 61, 63, 70, 71, 75 and 76). One of ordinary skill in the art would have been motivated to form the bone graft material of Piez et al into any desired shape, including those listed above, in order to better fit the bone graft to the osseous void it will be engrafted to. For example, a semi-sphere shaped graft would be more desirable for replacing or repairing a rotator cup on a shoulder than a flat disk. One would have expected success forming the bone graft of Piez et al into any desired shape because Piez et al teach their bone graft can be made by pouring a slurry of the mixture of the collagen and calcium phosphate component into an appropriate container, wherein upon solidification the bone graft takes the form of the container; therefore the bone graft can be made into any shape that a container can be molded into. One skilled in the art would be able to make, or obtain, a mold in any desired custom-made shape.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 16, 17, 30, 31, 41, 42, 62-66, 72 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piez et al (US Patent 4,795,467), in light of Bachand, in view of Koblish et al (US

Patent 6,458,162), and further in view of Lin et al (US Patent 6,458,162) and Sanders et al (US Patent 5,290,289).

Piez et al teach bone grafts comprised of calcium phosphate mineral preparations (which applicant calls the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion) and collagen (which applicant calls a biocompatible, resorbable polymer) (See col. 2, ln 32-35). The calcium phosphate mineral material can include a variety of forms of calcium phosphate, including beta tricalcium phosphate SYNTHOGRAFT; SYNTHOGRAFT is a commercially available form of beta tricalcium phosphate (See col. 2, ln 59-68 & Bachand, Pg. 2). The collagen is preferably obtained from the same individual or from bovine sources in order to reduce immune responses and increase biocompatibility (See col. 1, ln 30-35). Piez et al also teach a method for restoring or repairing bone comprising placing into a bony space the bone graft material comprised of calcium phosphate and collagen (See col. 2, ln 48-52, col. 5, ln 23-35 & col. 7, ln 4-48). Piez et al teach bone marrow, blood and saline can also be applied to the graft material (See col. 5, ln 15-21). Additionally, Piez et al teach the graft material can be loaded into a container to provide a desired shape, Piez et al specifically teach block, square, and sheet shapes (See col. 4, ln 67-col. 5, ln 2).

Piez et al teach that the mesh size of the mineral particles is a result effective variable that directly effects the degree of porosity, the pore volume, and the ratio of collagen to reaction product. Therefore it would have been obvious to one of ordinary skill in the art to develop mineral particles of appropriate sizes to provide the bone graft material with macro-, meso- or microporosity, at least 70% porosity and for at least 80% of the composition to comprise calcium phosphate (e.g. 80:20 or 90:10 calcium phosphate to collagen mass ratios). See teachings above.

Though Piez et al teaches the collagen can come from a bovine source, they do not teach a specific kind or concentration of any particular type of bovine collagen. However, it would have been

obvious to one of ordinary skill in the art at the time the invention was made to use at least 85% fibrillar, reconstituted type I bovine collagen in the bone graft material of Piez et al. See teachings above.

Piez et al do teach the graft material can be loaded into a container to provide a desired shape, therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to form the graft into any desired shape, including a cylinder, disk, a sleeve shape or a half sleeve shape, wherein the cross section of the sleeve is in the shape of a crescent moon, semi-sphere, semi-tubular, torus, or in a shape to conform to the acetabulum or any other desired anatomical tissue structure. See teachings above.

Piez et al do not teach their graft to further comprise a mesh or plate comprised of a metal or polymer. However, Koblish et al teach a similar bone graft material comprising porous calcium phosphate that can be formed on, around, or immersed within a solid material, such as metal or polymers (See Koblish et al, col. 26, ln 56-col. 27, ln 57). The metals and/or polymer material provides support and increased structural integrity, especially in load-bearing grafts, such as in the spinal vertebrae. Suitable metals include stainless steel, titanium, silver, gold and other metals stable in the human body (See col. 27, ln 1-3) (Claims 16, 17, 30, 31, 41, 42, 62, 66 and 73).

Though Koblish et al do not teach nitinol or polyetheretherketone as possible materials for the metal or polymer material, it would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively use nitinol or polyetheretherketone as the metal or polymer material. One of ordinary skill in the art would have been motivated to use polyetheretherketone as the supporting material in the grafts of Koblish et al because Lin et al teach PEEK to have excellent mechanical properties and machinability, and PEEK materials have been shown to be suitable for implantation (See Lin et al, col. 5, ln 38-52). Similarly, one of ordinary skill in the art would have been motivated to nitinol as the supporting material in the grafts of Koblish et al because Sanders et al teach that nitinol is especially suitable for implantation and has particular applicability in augmenting or restoring damaged

spinal vertebrae that are misshaped, due to its ability to "remember" its designated shape (See Sanders et al, col. 4, ln 13-47). One would have expected success using either PEEK or nitinol as the metal material in the graft of Koblish et al because Koblish et al teach that any metal stable in the human body can be used, and Lin et al and Sanders et al teach that PEEK and nitinol, respectively, are suitable for use in human implantation.

Though Koblish et al do not describe a mesh composite, it would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively use a mesh material in place of a solid material. One of ordinary skill in the art would have been motivated to use a mesh material in order to allow for less restricted flow of biological materials, such as osteocytes and blood flow into and out of the graft. One would have expected success because a strong mesh would provide similar support as solid material, and one of ordinary skill in the art would know how to perform such substitution.

It would have further been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the metal or polymer mesh or plate of Koblish et al, which can be modified in view of Lin et al or Sanders et al to comprise PEEK or nitinol material, into the bone graft of Piez et al in order to improve structural stability and provide additional support to the bone graft of Piez et al. The skilled artisan would have been motivated to add a metal or polymer mesh or plate component to the bone graft of Piez et al in order to provides support during development of the bone graft, and to provide increased stability and structural integrity to the bone graft after implantation. One would have been motivated to have the mesh or plate immersed within the bone graft of Piez et al when the bone graft is large in size, for example, in long bone grafts (Claim 65). Similarly, one would have been motivated to affix the mesh to the surface of a sleeve shaped graft in order to maintain structural integrity once implanted (Claims 64 and 72). One would have expected success applying the metal or polymer plate or mesh of Koblish et al to the grafts of Piez et al because both grafts are made from substantially similar materials in similar methods, and Koblish et al teach successful incorporation of the metal or polymer supports to the grafts;

therefore one would expect similar success performing the same incorporation of the metal or polymer grafts into the grafts of Piez et al.

Finally, it would have further been obvious to one of ordinary skill in the art at the time the invention was made to shred the graft material of Piez et al (Claim 63). One would have been motivated to shred the graft material of Piez et al in order to fill a metal or polymer body housing, such as those described by Koblish et al, with the bone graft shreds. By shredding the bone graft material one can increase the pore volume of the graft, therefore allowing for increased pore volume for ingrowth of autogenous bone and blood cells. Filling a housing with shredded bone grafts provides a prosthesis with the appropriate bone graft material, but wherein the structural integrity comes exclusively from the housing. Shredding the bone graft material and depositing the shreds in a solid housing would be a desirable means to utilize pieces of left over bone graft materials that are not large enough to act as a complete, solid graft, but rather can be shredded and packed in housing. One would have expected success because shredding the bone graft material of Piez et al could be done by such simple methods as processing left over pieces in a blender.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 70, 71 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sapiesko et al (US Patent 6,383,519).

Sapiesko et al teach a porous, shaped, inorganic bodies comprising biocompatible, resorbable polymers, such as gelatin, and the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent and at least one oxidizable precursor anion (See col. 4, ln 3-34). In preferred embodiments the oxidation-reduction reaction product is beta tricalcium phosphate (See col. 8, ln 28-46). The composition of Sapiesko et al can be used as bone graft material (See col. 5, ln 7-9). The bone graft

material of Sapiesko et al exhibits macro-, meso- and microporosity, and the material has a pore volume of at least 75% (See col. 9, ln 39- col. 10, ln 25). The graft material can be formed into a variety of shapes, including blocks, disks, cylinders, or sleeves for orthopedic surgery (See col. 12, ln 1-13; col. 23, ln 63-65; col. 42, ln 64-67).

Sapiesko et al teach the bone graft material can be custom tailored based on the absorbent material chosen as the initial support or by custom carving a desired shape out of a large block of the graft material (See col. 12, ln 25-30 and 42, ln 64-67); therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to form grafts in the shape of sleeves, wherein the cross-section of the sleeve is in the shape of a crescent moon, or shapes selected to conform to mammalian, anatomical tissue structure, for example in the shape of a semi-sphere, semi-tubular, or torus (Claims 70, 71 and 75). One of ordinary skill in the art would have been motivated to custom tailor the grafts of Sapiesko et al into any desired shape, including those listed above, in order to better fit the bone graft to the osseous void it will be engrafted into/onto. For example, a semi-sphere shaped graft would be more desirable for replacing or repairing a rotator cup on a shoulder than a flat disk. One would have expected success forming the bone graft of Sapiesko et al into any desired shape because Sapiesko et al teach the shape of the bone graft is determined by the shape of the absorbent material chosen as the initial support. In their examples Sapiesko et al use materials as pliable as kitchen sponges; one of ordinary skill in the art would be able to manipulate the shape of these initial support materials, either by placing in a mold or by cutting, to the desired shapes, including sleeves, wherein the cross-section of the sleeve is in the shape of a crescent moon, or shapes selected to conform to mammalian, anatomical tissue structure, for example in the shape of a semi-sphere, semi-tubular, or a torus.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 16, 17, 30, 31 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cornell et al (J Ortho Trauma, 1991).

Cornell et al teach use of Collagraft (Zimmer Corporation, Warsaw, IN) as a bone graft material for filling open comminuted fractures by placing the Collagraft into the opened bony space. Collagraft comprises a composite of porous calcium phosphate and collagen (See Pg. 2). The calcium phosphate composite consists of 65% hydroxyapatite and 35% tricalcium phosphate. The pore volume is approximately 70%. The collagen is highly purified, completely resorbable, fibrillar bovine-derived collagen; it is 95% Type I bovine collagen (See Pg. 2 and 5). The Collagraft bone graft material is wetted with bone marrow aspirate before implantation.

Cornell et al also teach that the Collagraft bone graft material has no structural strength, and therefore all fractures were treated by internal and/or external fixation in conjunction with the Collagraft (See Pg. 2). Though Cornell et al do not specify what type of internal support was commonly used with the Collagraft bone grafts, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a mesh or a plate comprised of metal or a polymer as an internal support in conjunction with the Collagraft bone grafts. One of ordinary skill in the art would have been motivated to use a mesh or a plate comprised of metal or a polymer as an internal support in conjunction with the Collagraft bone grafts in order to provide structural support to the graft. Cornell et al specifically teach that such internal supports are needed and commonly used in conjunction with Collagraft bone grafts. One would have expected success using a metal or polymer mesh or plate support because Cornell et al teach internal supports are commonly used, and one of ordinary skill in the art would be able to choose an appropriate metal or polymer material acceptable for long term in vivo use. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 12, 13, 18, 27, 32, 44, 48, 50, 58, 59, 63, 67, 71 and 74 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-6, 11, 20, 23, 28, 37 and 40 of copending Application No. 10/973,781. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending application 10/973,781 are drawn to a method comprising placing a bone restorative in a bony space, wherein the bony restorative comprises a biocompatible, resorbable polymer, the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion, wherein the polymer is collagen, and wherein the reaction product is calcium beta tri-phosphate. The bone restorative material in the copending application is additionally imbibed with a therapeutic material, which is not required by the current application; however, it would have been obvious to one of ordinary skill in the art, at the time the current invention was made, to additionally imbibe the bone graft material with a therapeutic material, such as bone morphogenic protein or various other growth factors in order to encourage ingrowth of natural osteocytes and blood cells into the bone graft. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 2, 12-18, 27-32, 39-42, 44, 48-50, 58-67 and 70-76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 11-17, 21-25, 29-32, 36-41 and 45-49 of copending Application No. 10/973,972. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application describe a bone restorative foam material comprising biocompatible, resorbable polymer and the reaction product of an oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion, wherein the polymer is collagen, and wherein the reaction product is beta tri-phosphate, it has macro-, meso- and microporosity, it further comprises a mesh, wherein the mesh is titanium, stainless steel, nitinol, a composite polymer, or polyetheretherketone, it has a cylindrical, block, wedge, sheet, hemisphere, half pipe, rod, funnel, or discoid shape, and presumably could be molded into any desired shape, and is also wetted with a fluid comprising bone marrow aspirate, blood or saline. Though the bone restorative material of the copending application comprises an osteoconductive foam, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the currently claimed bone graft material in a foam form in order to more easily and effectively fill osseous voids with minimal invasion. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER